REMARKS/ARGUMENTS

1. Indication of Allowability

Applicants acknowledge with appreciation the indication by the Examiner that the elected species was deemed free of the prior art.

2. Rejection Under 35 USC 102(b) Based on Expanded Search

Based upon the finding that Applicants' elected species is allowable, the Examiner conducted a further search based upon a compound defined where $R_1 = C_1$ alkyl substituted with a 6-membered ring; $R_2=R_4$; $R_3=C_1$ alkyl; R_5=carbonyl; L=a chain of 5 atoms; and M= a substituent capable of complexing with a protein (-C(O)NHOH).

Based on the Examiner's further search, the Examiner rejected claims 1-119 under 35 USC 102(b) as being anticipated by Peptide Science (1999), Volume Date 1988, 35th, p. 181-184 ("Peptide Science").

A. Complete Copy of Peptide Science Reference Provided

In regard to the Peptide Science reference that the Examiner bases his rejection, a complete copy of the reference is enclosed as Exhibit A. As can be seen in the complete copy of the reference, the compound that appears in the abstract is Ac-L-Asu(NHOH)-NHBzl which appears in Table 1 of page 183 as Compound 10. Reliance on the actual reference is respectfully requested in the future.

B. HDAC Activity of Ac-L-Asu(NHOH)-NHBzl is Inferior To Cyclic Tetrapeptides

As can be seen in Table 2, the HDAC inhibitory activity of Ac-L-Asu(NHOH)-NHBzl (Compound 10) is substantially inferior to that of trichostatin A and the cyclic tetrapeptides taught by the Peptide Science reference. The next to last paragraph on page 184 of the reference teaches that

> [a] reference compound (10) was also synthesized to elucidate the importance of [the] cyclic tetrapeptide framework. Inhibitory activity of 10 was decreased by two orders of magnitude than Asu(NHOH) containing cyclic tetrapeptides except 5.

With this teaching, the Peptide Science reference teaches away from inhibitors that do not have a cyclic tetrapeptide structure.

C. R_4 excluded from being hydrogen

As can be seen in Table 1 of the Peptide Science reference, the compound in the "A" position of the cyclic tetrapeptide is always a compound that possesses a secondary as opposed to a tertiary nitrogen (i.e., the nitrogen atom has a hydrogen substituent). Accordingly, the subsitutent that the Examiner appears to deem analogous to R_4 is always taught to be hydrogen. Hence, there is no teaching or suggestion that the hydrogen on the nitrogen of Compound 10, L-Api(NHOH), L-Asu(NHOH), or L-Aaz(NHOH) may be substituted with a substituent other than hydrogen.

Independent claims 41, 117 and 119 already exclude R_4 from being hydrogen. Applicants amend independent claims 61, 79, 100, 101, 104, 110, 113, and 116 to exclude R_4 from being hydrogen and also add new claims 120-124 which depend from independent claims 101, 104, 110, 113 and 116 *(Note remarks below in Section D)* which specify that R_4 is not hydrogen. In view of these amendments and the new claims, the Examiner's rejection for anticipation based on the Peptide Science reference is overcome.

D. Cinnamate Moiety As L Distinguishes Reference

The Peptide Science reference is focused on substituting the epoxiketone of trapoxin B with the hydroxamic acid of trichostatin A. There is no teaching, however, to modify the C_5 alkyl chain attaching the epoxiketone and hydroxamic acid moieties to the cyclic tetrapeptide.

Applicants also draw the Examiner's attention to independent claims 101, 104, 107, 110, 113, 116, and 119 and dependent claims 57, 76, and 97 which specify that L is a cinnamate moiety.

Applicants submit that the Peptide Science reference does not provide any teaching or suggestion that the C_5 alkyl chain may be replaced with a cinnimate moiety. Furthermore, as noted in Section B above, the Peptide Science reference teaches the criticality of the cyclic tetrapeptide structure which is not present in the compounds that are being claimed. In view of this clear distinction, Applicants respectfully request further acknowledgement of the novelty of these independent and dependent claims over the Peptide Science reference.

CONCLUSION

Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,
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